concerned. A confirmatory DNA test would prevent this situation.

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NECROTISING ENTEROCOLITIS AS AN INFECTIOUS DISEASE — EVIDENCE FROM AN OUTBREAK OF INVASIVE DISEASE DUE TO EXTENDED-SPECTRUM BETA-LACTAMASE-PRODUCING *KLEBSIELLA PNEUMONIAE*

To the Editor: Necrotising enterocolitis (NEC) is a severe gastro-intestinal disorder, predominantly seen in hospitalised low-birth-weight newborn infants. It is associated with significant morbidity and mortality. Infants with NEC require parenteral nutrition and intravenous antibiotics with prolongation of hospitalisation. Severe cases require surgical resection of necrotic bowel wall with the attendant problems of the short gut syndrome.[1] NEC places an enormous burden on resource-poor institutions.

We recently documented an outbreak of invasive disease due to extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* (ESKP).[2] The majority of patients had concomitant NEC. Rotavirus, a well-described risk factor for NEC,[3] and endemic in the neonatal wards, was also implicated.

The aims of this study were twofold: firstly to investigate the relationship between ESKP, rotavirus and NEC in a cross-sectional study, and thereafter to determine whether the implementation of improved infection control measures was associated with a reduction in the incidence of NEC.

Diagnosis of necrotising enterocolitis. The presence of any of the following criteria: mild abdominal distension, feeding intolerance or vomiting were regarded as 'suspected NEC'. Dilated 'sausage-shaped' bowel loops or thickened bowel loops seen on abdominal radiography were regarded as supportive evidence for suspected NEC. For 'confirmed NEC' any of the following clinical criteria were diagnostic: severe abdominal distension, occult blood in stool, bile-stained vomiting, persistent ileus, pneumatosis intestinalis or bowel perforation requiring surgical intervention.[4]

Survey for rotavirus and ESKP. Stool specimens from all patients in both intermediate care wards were submitted for rotavirus detection in a cross-sectional survey. Bi-weekly rectal swabs from all patients were submitted for ESKP culture as part of the infection control strategy.

Microbiology and virology. Rectal swabs were taken on dry, cotton-tipped swabs. Stool samples were collected in sterile containers. All swabs were cultured on McConkey medium (Biolab Diagnostics, Midrand, RSA) supplemented with cefotaxime 0.5 mg/l, selecting organisms resistant to third-generation cephalosporins.[5] Identification of *K. pneumoniae* was verified by dehydrolisation of arginine, decarboxylation of lysine or ornithine and the ability to utilise citrate. Extended-spectrum beta-lactamase (EsβL) producers were verified by the double disc diffusion test described by Jarlier *et al.*[6] Stool specimens were assayed for rotavirus and adenovirus 40 and 41 by enzyme-linked immunosorbent assay (Rotaclone and Adenoclone, Cambridge Biotech, Worcester, UK).

Influence of infection control measures on admissions to the neonatal intensive care of patients with confirmed NEC. To evaluate the impact of improved infection control, two analyses were undertaken. Firstly, the number of patients with 'confirmed' NEC admitted to the neonatal intensive care unit (NICU) before and after the implementation of infection control measures were compared. These included premature infants from the intermediate care neonatal wards, temporary wards opened to accommodate infants during renovations, and those transferred from elsewhere. Because the nadir of both NEC and ESKP colonisation was in September 1996, an equivalent number of NICU admissions before and after 30 September 1996 were analysed. Because 'suspected' NEC can be confused with feeding intolerance, we considered that patients requiring admission to the NICU because of severe NEC would be a valid reflection of change in incidence in the intermediate care wards. The incidence of NEC in the intermediate care wards was also compared for the same two time periods. Information was obtained from a database maintained by the neonatology section of the hospital and from the hospital's Medical Informatics unit.

Although compliance of health care workers with infection control measures was not monitored, regular meetings with nurses were held on a bi-monthly basis after the institution of infection control measures to reinforce the importance of infection control.

Statistical analysis. Chi-square analysis and odds ratio (OR) were calculated using Epi Info version 6.03, Center for Diseases Control, Atlanta, Georgia, USA.

Cross-sectional survey. The cross-sectional survey for rotavirus was conducted over a 4-day period from 19 to 24 August 1996, and results are shown in Table I. Rotavirus was detected in 35 of 44 samples (79.5%) and adenovirus type 40/41 in none. Thirty-one infants (70.5%) were colonised with both rotavirus and ESKP simultaneously. Thirteen infants (29.5%) of the 44 surveyed had either confirmed or suspected NEC. Ten of the 13 (77%) had isolation of both ESKP and rotavirus.

Table I. Cross-sectional survey for rotavirus and extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* in 44 low-birth-weight infants hospitalised in intermediate care wards

	Number	%
Rotavirus-positive	35	79.5
ESKP-positive	35	79.5
Rotavirus- and ESKP-positive	31	88.6
Patients with NEC*	13	29.5
Patients with NEC and positive for rotavirus and ESKP	10	77

* Four patients had suspected and 9 confirmed NEC.
ESKP = extended-spectrum beta-lactamase-producing *K. pneumoniae*; NEC = necrotising enterocolitis.

As a further analysis of the extent of ESKP colonisation in the intermediate care wards, a comparison was made for first month of initial intervention and the same month a year later, once infection control practices were perceived to be well implemented. In August 1996, 39% of admissions to the intermediate care wards became colonised with ESKP. In August 1997 only 20% of admissions became colonised (OR 2.92, $P = 0.000006$), suggesting that colonisation during the outbreak was excessive and that infection control practices had been at least partially effective.

Improved infection control associated with a reduction in NEC. From 1 January to 30 September 1996, 35 (12.8%) of 239 infants were admitted from the intermediate care wards for management of severe NEC. From the beginning of October 1996 through April 1997, 18 (6%) of 298 admissions were for NEC. This represents a decline of more than 50% ($P = 0.0085$) (Table II). A comparative analysis of ICU admissions for NEC from January through September 1994 and October through April 1995 showed incidences of 2.9% and 3.9% respectively (OR 0.75, $P = 0.5$).

Table II. The influence of improved infection control practice on patients with confirmed NEC admitted to the neonatal intensive care unit

	Admissions to the neonatal intensive care unit (*N*)	Patients with NEC admitted to the intensive care unit (%)
Period of study		
January - September 1996	239	35 (12.8)
October 1996 - April 1997	298	18 (6)

Odds ratio 2.28 (1.21 - 4.31), $P = 0.0085$.

Discussion

The present study provides strong evidence that NEC is, in part, an infectious disease. NEC has been shown to occur in clusters, often associated with outbreaks of nosocomial disease.[7] We demonstrated an extremely high incidence of stool colonisation with both ESKP and rotavirus in our cross-sectional survey and a reduction in ESKP colonisation a year later, thus demonstrating poor compliance with handwashing and other infection control practices and subsequent improvement. The high prevalence of dual colonisation in patients with NEC suggests either a causal relationship or that another unidentified hand-transmissable agent might be implicated.

Additional evidence implicating a transmissable agent in NEC is the significant reduction in number of patients with confirmed NEC from the intermediate care wards requiring transfer to the NICU after the implementation of improvements in infection control. A similar experience was reported 20 years previously. Book *et al.*[8] first demonstrated a reduction in NEC simultaneous to the improvement of infection control practices in a study from Utah, USA. Stein[9] also noted a reduction in NEC in premature infants at Baragwanath Hospital in Soweto, South Africa after a reduction in nosocomial gastro-enteritis and salmonellosis.

NEC probably has a multifactorial aetiology. Risk factors include prematurity, immunological immaturity, immature intestinal epithelial barrier, aggressive enteral feeding, formula feeding and hypoxia-ischaemia.[10] Infectious agents probably act as co-factors, explaining the inability to link a specific pathogen with NEC. Panigrahi *et al.*[11] have implicated bacterial adherence to enterocytes, possibly explaining why diverse bacteria have been implicated. A recent report[12] has documented that *K. pneumoniae* may be entero-invasive, thus providing another mechanism for causing NEC. In our study, we screened for ESKP only and not for sensitive organisms because of ease of detection of resistant organisms. Sensitive organisms were suppressed by addition of cefotaxime to the culture medium, thus permitting rapid screening in a busy laboratory setting. Organisms that are sensitive to extended-spectrum cephalosporins are as likely to be implicated as ESKP.

In conclusion, infection control measures that include adequate hand hygiene are potent factors in prevention of NEC.

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CHILDHOOD ACUTE VIRAL HEPATITIS IN CAPE TOWN

To the Editor: Most episodes of acute viral hepatitis (AVH) are easily recognised. Of the hepatitis viruses hepatitis A, hepatitis B and hepatitis E (HA, HB, HE) are most likely to cause the typical syndrome. In South Africa, serological surveys have suggested that HA infection occurs in early childhood in poor communities, but that many adults in wealthier communities remain susceptible.[1,2] HB is mainly acquired in childhood.[3] The epidemiology of HE is only partly known.[4]

In childhood, AVH is usually uncomplicated and self-limited and no therapy is required. It is not possible to identify the agent responsible without serological or virological tests. It is also not possible to predict which child will run a complicated course.

In the light of this, the policy of the Red Cross War Memorial Children's Hospital (RCCH) Medical Outpatients' Department (MOPD), which largely serves children from poor Cape Town communities, has been to perform liver function and serological tests only on children attending with AVH who have special epidemiological circumstances (such as the institutionalised child) or suspected complications.

A number of factors led to a review of this policy. The options for HA and HB prophylaxis for contacts have changed with the advent of vaccines. Since 1995 all infants have been immunised against HB.[5]

This study represents part of an attempt to arrive at an appropriate policy on the management of children with AVH in this and similar settings. The study aimed to examine the demography and pattern of diagnosis, referral, complications, and notification of children with AVH.

Patients with AVH attending the RCCH during 1996 (the last complete year during which unreferred non-urgent patients were seen at the hospital) were studied. Data were assembled from computerised records of visits to the MOPD by patients with viral hepatitis (using the *International Classification of Diseases* 9 (ICD 9), Code 070),[5] inpatients with a discharge diagnosis of viral hepatitis or hepatic coma (*ICD 9* Code 572.2), patients with positive HA immunoglobulin M (IgM) tests (identified from laboratory results) and the hospital register of notifications. Patients with chronic HB were excluded after review of the clinical records of patients with HB (*ICD 9* Codes 070.2 and 070.3). Serious complications were explored by examining the clinical records or discharge summaries of inpatients. A notification rate was calculated by comparing the notification register with the whole data set.

Table I shows the race, sex and age composition of the 326 patients. The median age was 70 months and the maximum 14 years. Two hundred and seventy-two of the outpatients (83.4%) were self-referred. Analysis of postal codes showed that the areas that patients came from reflected the usual drainage areas for the MOPD, but formerly 'black' areas were underrepresented compared with formerly 'coloured' areas (ratio 1:6). The ratio for all patients who attended the MOPD in 1996 was 1:2. Whether this indicates differing patterns of self-referral for jaundice or a genuinely lower rate of symptomatic AVH among black children cannot be ascertained from these data.